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MSU 4.1-541
11/05/2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Muraleedharan G. Nair, Haibo Wang, Gale M. Strasburg, Alden M. Booren and James I. Gray

Serial No.: 09/761,143 Group Art Unit: 1651

Filed : January 16, 2001

For : METHOD FOR INHIBITING CYCLOOXYGENASE AND INFLAMMATION USING CYANIDIN

Examiner : P. Patten

Assistant Commissioner For Patents

Washington, D. C. 20231

RESPONSE UNDER 37 CFR 1.112

Sir:

This is in response to the Office Action mailed August 5, 2002:

Claims 1, 3 to 6, 27 to 30 and 34 were rejected under 35 USC 103(a) as being unpatentable over Lietti et al (GB 1,598,294) in view of Wurm et al (1982). This combination of references is identical to the rejection which was discussed in Applicants' Brief on Appeal.

Wurm et al is dealing with different flavonoids which are not anthocyanins. The reference does not even disclose cyanidin. The structure of the flavonoids defined by the authors is clearly specified in Wurm et al. Also see page 4, lines 26 to 34 of the Applicants' specification where it states that the C_2-C_3 double bond

is important in the anthocyanins. A rejection cannot impute a teaching to a reference which does not exist. Wurm et al is thus not an effective reference.

Lietti et al is concerned with cyanidin. The statement in Lietti et al that cyanidins are hydrolyzed chemically is then taken to mean that this occurs in vivo in the following unsupported sentence:

> "Thus, that *in vivo*, anthocyanins are all converted (hydrolyzed) to the non-glycosylated anthocyanidins before entry into the intestinal tract" (emphasis added).

This statement is unsupported by Lietti et al. Further, it is pure speculation, which is also incorrect. Enclosed is a copy of an article which was recently published by Milbury et al (Mechanisms of Ageing and Development 123 997-1006 (2002) which demonstrates beyond a doubt that at least some of the anthocyanins in the glycosylated form find their way into the blood stream of the humans tested. The compound tested was cyanidin 3-glucoside.

Claims 1, 3-6, 15-18,27-30 and 34 were rejected under 35 USC 103(a) over the above references further in view of Heckert et al (U.S. Patent No 5,516,535). Lietti et al and Wurm et al have been discussed and the same arguments apply. Heckert et al do not overcome the defects of the previous references. Heckert discloses beverages for providing bioavailable β-carotene which in particular embodiments can be fiber-supplemented. Sources of fiber include pulp, such as orange pulp.

Heckert et al do not teach or suggest that the beverages provide anthocyanins or cyanidin as in the claimed method. While the beverages contain some fruit juice, fruit juice is not the primary constituent of the beverages. When Heckert et al is viewed as a whole, a person of ordinary skill in the art would be led to believe that the purpose of the fruit juice in the beverage is to provide flavor, not to inhibit the enzymes or inflammation as in the claimed method. A person of ordinary skill in the art would also conclude that it would be unlikely that the beverages contain significant amounts of anthocyanins and/or cyanidin. Reconsideration is requested.

Applicants respectfully submit that the 35 USC § 112 rejection of Claims 1, 3-6, 15-18, 27-30 and 34 as new matter continues to be improper. In addition, there is no new basis for this rejection and as such, applicants submit that this issue is ready for appeal. More particularly, applicants are claiming the combination of an anthocyanin and cyanidin to reduce inflammation or inhibit the COX enzymes. There is more than sufficient disclosure in the application to support this particular combination for both claimed purposes. It is not necessary that an example be provided for each and every combination. As stated by the U.S. Court of Customs and Patent Appeals, in the *Application of Hogan*, 194 U.S.P.Q. 527, 559 F.2d 595, "[t]his court has held that claimed subject matter need not be described *in haec*

verba ("in the same words", Black's law Dictionary) in the application to satisfy the written-description-of-the-invention requirement. (Citing In re Smith, 481 F.2d 910, 914 (CCPA 1973).) In *Application of Hogan*, applicants' claim directed to a homopolymer having a melting point in the range of 390 to 425°F was rejected as new matter by the Examiner. The CCPA reversed this new matter rejection on the basis that appellants taught that they had "produced crystalline polymers of 4-methyl-1-pentene which have melting points in the range of 390 to 425°F." and that one skilled in the art reading this statement that would reasonably conclude that "polymers of 4-methyl-1-pentene" describes homopolymers of 4-methyl-1-pentene because that is the "necessary and only reasonable construction" to be given this statement. (citing Vogel v. Jones, 486 F.2d 1068, 1075 (CCPA 1973); Binstead v. Littmann, 242 F.2d 766, 770, 44 CCPA 839, 844 (1957)). Therefore, even though the appellants' specification did not include a single sentence that taught the combination of a homopolymer and a specific melting point, the CCPA found that this combination could be inferred and was therefore, not new matter. In the present application, it is not even necessary to make any inferences to arrive at the claimed combination. The specification teaches that the "mixture of anthocyanins, bioflavonoids, and phenolics can be tableted and used as a natural nutraceutical, phytoceutical, or dietary supplement." (See page 8, lines 27-30) This mixture is

again taught in original claim 15. Since "mixture" is not limited to requiring at least two of the general types of compounds, it follows that the mixture could be comprised of two or more different types of anthocyanins or two or more different types of bioflavonoids. Moreover, since anthocyanin is clearly described in the instant specification as including cyanidin within the broad category of anthocyanin, (See page 5, line 37 to page 6, line 3) the only logical way to claim this combination is to use the terms "anthocyanin" for describing the glycosolated forms of this general category of compounds and cyanidin for the aglycone form of this general category. In view of the above, applicants respectfully submit that the § 112 new matter rejection is improper and should be withdrawn. Alternatively, applicants submit that this issue is ready for appeal and must be advanced to this stage unless the Examiner withdraws this rejection.

Claims 1, 3 to 6, 15 to 18, 27 to 30 and 34 were again rejected under 35 USC 112, first paragraph. This is the same rejection which was appealed. The application clearly contemplated that the term anthocyanins included cyanidin (see page 5, line 37 to page 6, line 3). Page 1, lines 35 to page 3, line 3, shows that cherries contain a mixture including cyanidin. Figure 1 shows the structures of the glycosylated anthocyanins. Cyanidin is disclosed at page 6, lines 26 to 29 in the context of Figure 1. The "anthocyanins" are

discussed at page 8, line 27 to page 9, line 5 of the specification. The anthocyanins alone are discussed as not having significant activity *in vitro* against PGHS-1 and PGHS-2 at low concentrations. At higher concentrations the color interferes with the *in vitro* test as does the fact that the cyanidin glycosides are strong oxidants. *In vivo* the combination of cyanidin and the glycosides of cyanidin (See related U.S. Patent No. 6,194,469 to Nair et al and assigned to the assignee of the present application) at least provides antioxidant activity and PGHS-1 and PGHS-2 inhibition.

It is now believed that Claims 1, 3 to 6, 15 to 18, 27 to 30 and 34 are in condition for allowance. Notice of Allowance is requested.

Respectfully,

By: _____
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Enclosure: Milbury, et al., Mechanisms of Ageing and Development 123 997-1006 (2002).

GP 1651

Practitioner's Docket No. MSU 4.1-541 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Muraleedharan G. Nair, Haibo Wang, Gale M. Strasburg, Alden M. Booren and James I. Gray

Application No.: 09/761,143 Group No.: 1651

Filed: January 16, 2001 Examiner: P. Patten

For: METHOD FOR INHIBITING CYCLOOXYGENASE AND INFLAMMATION USING CYANIDIN

Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT TRANSMITTAL

1. Transmitted herewith is an amendment for this application.

STATUS

2. Applicant is
   - ☐ a small entity. A statement:
     - ☐ is attached.
     - ☐ was already filed.
   - ☒ other than a small entity.

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10*
(When using Express Mail, the Express Mail label number is mandatory; Express Mail certification is optional.)

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a) **37 C.F.R. § 1.10 ***

☒ with sufficient postage as first class mail. ☐ as "Express Mail Post Office to Addressee" Mailing Label No. _____ (mandatory)

TRANSMISSION

☐ facsimile transmitted to the Patent and Trademark Office, (703) _____-_____

Tammi L. Taylor
Signature

Date: 11/05/2002

Tammi L. Taylor
(type or print name of person certifying)

** Only the date of filing (§ 1.6) will be the date used in a patent term adjustment calculation, although the date on any certificate of mailing or transmission under § 1.8 continues to be taken into account in determining timeliness. See § 1.703(f). Consider "Express Mail Post Office to Addressee" (§ 1.10) or facsimile transmission (§ 1.6(d)) for the reply to be accorded the earliest possible filing date for patent term adjustment calculations.*

EXTENSION F TERM

NOTE: "Extension of Time in Patent Cases (Supplement Amendments) — If a timely and complete response has been filed after a Non-Final Office Action, an extension of time is not required to permit filing and/or entry of an additional amendment after expiration of the shortened statutory period.

If a timely response has been filed after a Final Office Action, an extension of time is required to permit filing and/or entry of a Notice of Appeal or filing and/or entry of an additional amendment after expiration of the shortened statutory period unless the timely-filed response placed the application in condition for allowance. Of course, if a Notice of Appeal has been filed within the shortened statutory period, the period has ceased to run." Notice of December 10, 1985 (1061 O.G. 34-35).

NOTE: See 37 C.F.R. § 1.645 for extensions of time in interference proceedings, and 37 C.F.R. § 1.550(c) for extensions of time in reexamination proceedings.

NOTE: 37 C.F.R. § 1.704(b) ". . .an applicant shall be deemed to have failed to engage in reasonable efforts to conclude processing or examination of an application for the cumulative total of any periods of time in excess of three months that are taken to reply to any notice or action by the Office making any rejection, objection, argument, or other request, measuring such three-month period from the date the notice or action was mailed or given to the applicant, in which case the period of adjustment set forth in § 1.703 shall be reduced by the number of days, if any, beginning on the day after the date that is three months after the date of mailing or transmission of the Office communication notifying the applicant of the rejection, objection, argument, or other request and ending on the date the reply was filed. The period, or shortened statutory period, for reply that is set in the Office action or notice has no effect on the three-month period set forth in this paragraph."

3. The proceedings herein are for a patent application and the provisions of 37 C.F.R. § 1.136 apply.

(complete (a) or (b), as applicable)

(a) ☐ Applicant petitions for an extension of time under 37 C.F.R. § 1.136 (fees: 37 C.F.R. § 1.17(a)(1)-(4) for the total number of months checked below:

Extension (months)	Fee for other than small entity	Fee for small entity
☐ one month	$ 110.00	$ 55.00
☐ two months	$ 400.00	$ 200.00
☐ three months	$ 920.00	$ 460.00
☐ four months	$ 1,440.00	$ 720.00

Fee: $_____

If an additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

☐ An extension for _____ months has already been secured. The fee paid therefor of $_____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request $_____

OR

(b) ☒ Applicant believes that no extension of term is required. However, this is a conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition for extension of time.

FEE FOR CLAIMS

4. The fee for claims (37 C.F.R. § 1.16(b)-(d)) has been calculated as shown below:

	(Col. 1)		(Col. 2)	(Col. 3)	SMALL ENTITY			OTHER THAN A SMALL ENTITY	
	CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NO PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDIT. FEE	*OR*	RATE	ADDIT. FEE
TOTAL	* 14	MINUS **	20	= −0−	x$9=	$		x$18=	$ −0−
INDEP.	* 2	MINUS ***	3	= −0−	x$42=	$		x$84=	$ −0−
☐ FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					+$140=	$		+$280=	$ −0−
					TOTAL ADDIT. FEE	$	*OR*	TOTAL ADDIT. FEE	$ −0−

* If the entry in Col. 1 is less than entry in Col. 2, write "0" in Col. 3.
** If the "Highest No. Previously Paid for" IN THIS SPACE is less than 20, enter "20."
*** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 3, enter "3."
The "Highest No. Previously Paid For" (Total or indep.) is the highest number found in the appropriate box in Col. 1 of a prior amendment or the number of claims originally filed.

WARNING: *"After final rejection or action (§ 1.113) amendments may be made cancelling claims or complying with any requirement of form which has been made." 37 C.F.R. § 1.116(a) (emphasis added).*

(complete (c) or (d), as applicable)

(c) ☒ No additional fee for claims is required.

OR

(d) ☐ Total additional fee for claims required $_____.

FEE PAYMENT

☐ Attached is a ☐ check ☐ money order in the amount of $_____

☐ Authorization is hereby made to charge the amount of $_____

- ☐ to Deposit Account No. _____
- ☐ to Credit card as shown on the attached credit card information authorization form PTO-2038.

WARNING: *Credit card information should not be included on this form as it may become public.*

☐ Charge any additional fees required by this paper or credit any overpayment in the manner authorized above.

A duplicate of this paper is attached.

FEE DEFICIENCY

NOTE: If there is a fee deficiency and there is no authorization to charge an account, additional fees are necessary to cover the additional time consumed in making up the original deficiency. If the maximum, six-month period has expired before the deficiency is noted and corrected, the application is held abandoned. In those instances where authorization to charge is included, processing delays are encountered in returning the papers to the PTO Finance Branch in order to apply these charges prior to action on the cases. Authorization to charge the deposit account for any fee deficiency should be checked. See the Notice of April 7, 1986, (1065 O.G. 31-33).

6. ☒ If any additional extension and/or fee is required, charge Account No. 13-0610

AND/OR

☒ If any additional fee for claims is required, charge Account No. 13-0610

Reg. No.: 20,931

Tel. No.: (517) 347-4100

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SIGNATURE OF PRACTITIONER

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(type or print name of practitioner)

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